Pending Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-28 (canceled).

Claim 29. (currently amended) A method for treating a mammal to resist early graft failure comprising,

a) introducing into cells of a graft from the mammal an effective amount of at least one nucleic acid encoding [at least] one of the following agents: endothelial cell protein C receptor (EPCR), thrombomodulin (TM), NF-κB inhibitor, or a functional fragment of the EPCR or TM ~~thereof~~; provided that when the agent is thrombomodulin, the nucleic acid further encodes ~~at least one of the endothelial cell protein C receptor (EPCR) or~~ the NF-κB inhibitor, wherein the introducing is performed *ex vivo* or by direct injection into the graft,

b) expressing the agent in the cells to increase activated protein C (APC); and

c) increasing the APC in the graft cells sufficient to resist the early graft failure, wherein,

(i) the functional fragment of the EPCR has at least about 85% of the protein C ~~activation~~ binding activity of human EPCR, and

(ii) the functional fragment of the TM has at least about 85% of the thrombin binding activity of human thrombomodulin~~, and~~

~~(iii) the functional fragment of the NF-κB has at least about 90% of the activity of IκB~~.

Claim 30. (currently amended) A method for engineering a vascular graft of a mammal to resist early failure, the method comprising:

a) introducing into cells of the graft from the mammal an effective amount of at least one nucleic acid encoding [at least] one of the following agents: endothelial cell protein C receptor (EPCR), thrombomodulin (TM), NF-κB inhibitor, or a functional fragment of the EPCR or TM ~~thereof~~; provided that when the agent is thrombomodulin, the nucleic acid further encodes ~~at least one of the endothelial~~

~~cell protein C receptor (EPCR) or~~ the NF-κB inhibitor, wherein the introducing is performed *ex vivo* or by direct injection into the graft,

b) expressing the agent in the cells to increase activated protein C (APC); and

c) increasing the APC in the graft sufficient to produce the engineered vascular graft,

wherein,

(i) the functional fragment of the EPCR has at least about 85% of the protein C ~~activation~~ binding activity of human EPCR,

(ii) the functional fragment of the TM has at least about 85% of the thrombin binding activity of human thrombomodulin~~, and~~

~~(iii) the functional fragment of the NF-κB has at least about 90% of the activity of IκB~~.

Claim 31. (previously presented) The method of claim 29, wherein the method further comprises transplanting the graft into the mammal.

Claim 32. (previously presented) The method of claim 29, wherein prior to step a) of the method, the graft is transplanted into the mammal.

Claim 33. (previously presented) The method of claim 29, wherein the method is performed on the graft *in vivo.*

Claim 34. (previously presented) The method of claim 31, wherein the transplanted vascular graft has sufficient APC activation as determined by a standard protein C assay to prevent or treat early graft failure.

Claim 35. (previously presented) The method of claim 34, wherein the level of protein C activation as determined by a standard protein C detection assay of the treated graft is at least about one order of magnitude higher than a control vessel.

Claim 36. (previously presented) The method of claim 35, wherein the higher protein C level of the treated vascular graft is detectable for at least about a week.

Claim 37. (previously presented) The method of claim 34, wherein the early graft failure is accompanied by thrombosis.

Claim 38. (previously presented) The method of claim 29, wherein the nucleic acid is inserted into a cassette.

Claim 39. (previously presented) The method of claim 38, wherein the cassette includes a promoter.

Claim 40. (previously presented) The method of claim 39, wherein the cassette is inserted into a vector.

Claim 41. (previously presented) The method of claim 40, wherein the vector comprises sequence from an adenovirus, retrovirus, or adeno-associated virus.

Claim 42. (previously presented) The method of claim 41, wherein the vector is a replication defective adenovirus.

Claim 43. (previously presented) The method of claim 29, wherein the nucleic acid encodes at least one other anticoagulant molecule.

Claim 44. (previously presented) The method of claim 43, wherein the anticoagulant molecule is thrombomodulin or a functional fragment thereof.

Claim 45. (previously presented) The method of claim 31, wherein the mammal is susceptible to an inflammatory or immunological stimulus and the method further comprises administering a therapeutic amount of at least one anti-coagulant, antithrombotic, or thrombolytic drug to treat or prevent that stimulus.

Claim 46. (previously presented) The method of claim 45, wherein the drug is administered before step a) or after step c) of the method.

Claim 47. (previously presented) The method of claim 46, wherein the anti-coagulant drug is coumadin.

Claim 48. (previously presented) An engineered vascular graft produced by the method of claim 30.

Claim 49. (previously presented) The engineered vascular graft of claim 48, wherein the vessel is an autologous saphenous vein graft (SVG).

Claim 50. (previously presented) The engineered vascular graft of claim 48, wherein the vessel is an arterial graft.

Claim 51. (previously presented) A kit for performing the methods of claims 29 or 30, the kit comprising:

a) one or more of the agents for increasing the activated protein C (APC),

b) means for detecting at least one of a) cell expression of the agents, and 2) the increased APC in the blood vessel; and

c) directions for using the kit.

Claim 52 (new) A method for treating a mammal to resist early graft failure comprising,

a) introducing into cells of a graft from the mammal an effective amount of at least one nucleic acid encoding at least one of the following agents: endothelial cell protein C receptor (EPCR), thrombomodulin (TM), NF-κB inhibitor, or a functional fragment of the EPCR or TM ; provided that when the agent is thrombomodulin, the nucleic acid further encodes at least one of the endothelial cell protein C receptor (EPCR) or-the NF-κB inhibitor, wherein the introducing is performed *ex vivo* or by direct injection into the graft, the nucleic acid being expressed from a recombinant adenovirus vector comprising a first adenovirus inverted terminal repeat (ITR) operably linked to the nucleic acid,

b) expressing the agent in the cells to increase activated protein C (APC); and

c) increasing the APC in the graft cells sufficient to resist the early graft failure, wherein,

(i) the functional fragment of the EPCR has at least about 85% of the protein C binding activity of human EPCR, and

(ii) the functional fragment of the TM has at least about 85% of the thrombin binding activity of human thrombomodulin.

Claim 53 (new) The method of claim 52, wherein the recombinant adenovirus vector further comprises a cytomeglovirus promoter operably linked to the nucleic acid.

Claim 54 (new) The method of claim 52 or 53, wherein the recombinant adenovirus vector further comprises a second ITR operably linked to the nucleic acid.

Claim 55 (new) The method of claim 52, wherein the recombinant adenovirus vector is AdTMh5.

Claim 56 (new) A method for treating a mammal to resist early graft failure comprising,

a) introducing into cells of a graft from the mammal an effective amount of at least one nucleic acid encoding at least one of the following agents: endothelial cell protein C receptor (EPCR), thrombomodulin (TM), NF-κB inhibitor, or a functional fragment of the EPCR or TM ; provided that when the agent is thrombomodulin, the nucleic acid further encodes at least one of the endothelial cell protein C receptor (EPCR) or-the NF-κB inhibitor, wherein the introducing is performed *ex vivo* or by direct injection into the graft, the nucleic acid being expressed from a recombinant adeno-associated virus (AAV) vector comprising operably linked to an adeno-associated virus inverted terminal repeat (ITR) and the nucleic acid,

b) expressing the agent in the cells to increase activated protein C (APC); and

c) increasing the APC in the graft cells sufficient to resist the early graft failure, wherein,

(i) the functional fragment of the EPCR has at least about 85% of the protein C binding activity of human EPCR, and

(ii) the functional fragment of the TM has at least about 85% of the thrombin binding activity of human thrombomodulin.

Claim 57 (new) The method of claim 56, wherein the AAV vector further comprises an operably linked Rous sarcoma virus long terminal repeat promoter.

Claim 58 (new) The method of claim 57, wherein the AAV vector is AAV_2 hTM.

Claim 59 (new) A method for treating a mammal to resist early graft failure comprising,

a) introducing into cells of a graft from the mammal an effective amount of at least one nucleic acid encoding at least one of the following agents: endothelial cell protein C receptor (EPCR), thrombomodulin (TM), NF-κB inhibitor, or a functional fragment of the EPCR or TM ; provided that when the agent is thrombomodulin, the nucleic acid further encodes at least one of the endothelial cell protein C receptor (EPCR) or-the NF-κB inhibitor, wherein the introducing is performed *ex vivo* or by direct injection into the graft,

b) expressing the agent in the cells to increase activated protein C (APC), the expression of the agent being sufficient to increase the activated protein C by about an order of magnitude higher than a control vessel as determined by a standard protein C assay; and

c) increasing the APC in the graft cells sufficient to resist the early graft failure, wherein,

(i) the functional fragment of the EPCR has at least about 85% of the protein C binding activity of human EPCR, and

(ii) the functional fragment of the TM has at least about 85% of the thrombin binding activity of human thrombomodulin.

Claim 60 (new) The method of claim 59, wherein the increased protein C activation in part b) is detectable for at least about one or two days.

Claim 61 (new) The method of claim 59, wherein the nucleic acid is expressed from a recombinant adenovirus vector comprising an adenovirus inverted terminal repeat (ITR) operably linked to and the nucleic acid.

Claim 62 (new) The method of claim 61, wherein the recombinant adenovirus vector further comprises a cytomeglovirus promoter operably linked to the nucleic acid.

Claim 63 (new) The method of claim 62, wherein the recombinant adenovirus vector further comprises a second ITR operably linked to the nucleic acid.

Claim 64 (new) The method of claim 63, wherein the recombinant adenovirus vector is AdTMh5.

Claim 65 (new) The method of claim 59, wherein the nucleic acid being is expressed from a recombinant adeno-associated virus (AAV) vector comprising an adeno-associated virus inverted terminal repeat (ITR) operably linked to the nucleic acid.

Claim 66 (new) The method of claim 65, wherein the AAV vector further comprises an operably linked Rous sarcoma virus long terminal repeat promoter.

Claim 67 (new) The method of claim 66, wherein the AAV vector is AAV_2 hTM.